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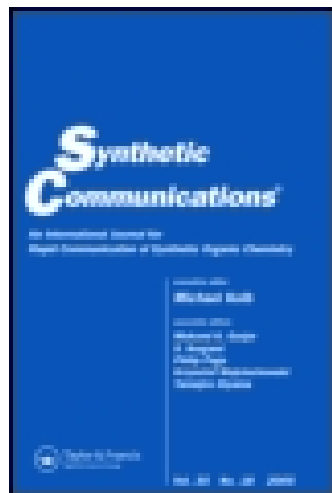
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### An Efficient Protocol for Synthesis of Pyrazolo[3,4-a]acridines

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# AN EFFICIENT PROTOCOL FOR SYNTHESIS OF PYRAZOLO[3,4-*a*]ACRIDINES

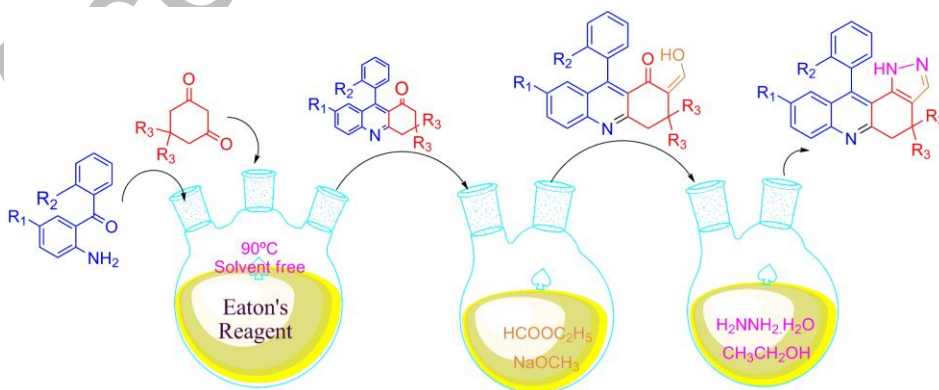
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## Abstract

A new class of pyrazolo[3,4-*a*]acridines have been prepared, the synthon acridones were obtained in very good yield by one pot reaction of 2-amino-5-chloro or nitro substituted benzophenones with 1,3-cyclic diketones in the presence of freshly prepared Eaton's reagent without solvent, using Friedländer synthesis. The intermediates were reacted with ethylformate followed by hydrazine hydrate to afford pyrazolo[3,4-*a*]acridines. All of the compounds were purified by recrystallization only, and no chromatographic work-up was required. The structures of the synthesized compounds were deduced by spectroscopic techniques, including single crystal X-ray diffraction.



**KEYWORDS:** Eaton's reagent, Friedländer synthesis, ethylformate, hydrazine hydrate, pyrazolo[3,4-*a*]acridines

## INTRODUCTION

Heterocyclic compounds, featuring an acridine scaffold, exhibit a wide variety of biological properties and functions and are of interest in organic chemistry. Acridine derivatives (ADs), known since the 19<sup>th</sup> century, were first used as pigments and dyes<sup>[1]</sup> and have been used for commercial purposes for more than a century. Several naturally occurring as well as synthetic ADs are known for antitumor,<sup>[2]</sup> antioxidant,<sup>[3]</sup> anticancer,<sup>[4]</sup> antimicrobial and antiparasitic activities. The acridine nucleus, condensed with additional heterocyclic rings, is also endowed with high cytotoxicity. Specifically, incorporation of five membered heterocyclic rings into the acridine chromophore strongly favors passive cellular drug uptake, rendering the efflux by MDR transporters inefficient.<sup>[5]</sup> The pyrazole nucleus is of interest for the development of new drugs, because of synthetic accessibility and diverse chemical and biological properties such as fungicidal, antimicrobial, anti-parasitic, anti-inflammatory, anticancer and antiviral activities.<sup>[6]</sup> Some pyrazoloacridine derivatives are known to fragment DNA through intercalation, causing apoptosis.<sup>[7]</sup> Within the pyrazoloacridine family, pyrazolo[3,4,5-*kl*]acridine (PZA, **I**) (**Figure. 1**) type of compounds containing electron deactivating nitro group proved to be a very exciting new class of antitumor agents, PZA is currently undergoing phase II clinical trials after exhibiting a broad spectrum of antitumor activities in preclinical *in-vivo* assays.<sup>[7,8]</sup> PZA displays solid tumor selectivity, activity against hypoxic cells and cytotoxicity in noncycling cells.<sup>[9]</sup> In addition, 4,5-

dihydropyrazolo[3,4-*a*]acridines were recently found to function as acetyl cholinesterase inhibitors.<sup>[10]</sup>

A well-known method for obtaining quinolines and related poly heterocycles involves the Friedländer quinoline synthesis. Known for more than a century, Friedländer synthesis<sup>[11]</sup> was applied to prepare quinoline derivatives by condensation of 2-aminoarylketones with carbonyl compounds possessing a reactive methylene group, followed by cyclodehydration<sup>[12]</sup>. Although considered the most useful method for the preparation of such a class of compounds, the synthetic protocols for polycyclic quinolines reported so far lead to low yields, extended reaction times, and dependence on harmful and often expensive catalyst systems, making the development of a simple, eco-friendly, low cost protocol desirable. We recently reported<sup>[13]</sup> cyclic imide synthesis using Eaton's reagent<sup>[14]</sup> (Phosphorus pentoxide-methanesulfonic acid) through cyclisation with Hydrazinylquinolines and cyclic anhydrides and successfully employed the Friedlander method on polycyclic quinolines by using Eaton's reagent.

Here we wish to report a practical and easy workup method for the synthesis of poly substituted quinolines using Eaton's reagent as alternative to Polyphosphoric acid (PPA) under solvent free conditions.

The reaction of 2-amino-5-nitrobenzophenone (**1a**) and 1,3-cyclohexanedione (**2a**) in the presence of freshly prepared Eaton's reagent (Phosphorus pentoxide-methanesulfonic acid) as a catalyst without solvent at 90°C afforded **3a** in 89% yield (**Scheme 1**). The IR

spectrum for **3a** shows an absorption band at  $1694\text{ cm}^{-1}$  due to the presence of the C=O group and a sharp band at  $1552\text{ cm}^{-1}$  confirmed the presence of the C=N group. The  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz) spectrum for **3a** shows a multiplet at  $\delta$  2.187-2.251 due to the  $\text{C}_3\text{-CH}_2$  protons, a multiplet at  $\delta$  2.665-2.698 due to the  $\text{C}_2\text{-CH}_2$  protons, and a multiplet at  $\delta$  3.334-3.366 due to the  $\text{C}_4\text{-CH}_2$  protons. The remaining aromatic protons appeared in the region of  $\delta$  7.109-8.435. The  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz) spectrum of **3a** shows the presence of 19 carbon signals.

In demonstrating efficiency and scope of Eaton's reagent for the synthesis of quinolines, cyclic ketones such as 1,3-cyclohexanedione and 5,5-dimethyl-1,3-cyclohexanedione smoothly condensed with 2-aminoaryl ketones to afford the respective polycyclic quinolines (**Scheme 2**). In most cases, the products were isolated by simple filtration and the crude products were purified by recrystallization from a mixture of ethylacetate and acetonitrile. All compounds (**Table. 1**) were isolated by recrystallization only and no chromatographic work-up was required to obtain pure products. The structures of **3a**, **3c**, and **3f** were confirmed by single crystal X-ray diffraction (**Figure.2, 3, & 4**).

Pyrazolo[3,4-*a*]acridines were synthesized from precursor polycyclic quinolones (**3**) and ethylformate. Sodium methoxide initiated the reaction, which took 4-5h at room temperature yielding exclusively (**4**), confirmed by TLC analysis (**Scheme 3**). After completion of the reaction, quenching with water dissolved the excess of sodium methoxide. Further purification via column chromatography was found to be unnecessary

(**Table. 2**). The structures of the derivatives **4a** and **4b** were confirmed by single crystal X-ray diffraction (**Fig.5 & 6**).

2-(hydroxymethylene)-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**4**) was reacted with hydrazine hydrate in ethanol for 2-3h (**Scheme. 4**), quenched with water and recrystallised in ethanol. The crude product obtained was recrystallised by using ethanol to give the pure product (**5a**). The IR spectrum of **5a** showed an absorption band at 3385 cm<sup>-1</sup> due to the presence of the NH group and two sharp bands at 1625 cm<sup>-1</sup> and 1554 cm<sup>-1</sup> associated with the presence of the C=N group. The <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) spectrum of **5a** shows a multiplet at δ 2.610-2.642 due to the C<sub>4</sub>-CH<sub>2</sub> protons, a multiplet at δ 3.083-3.267 due to the C<sub>5</sub>-CH<sub>2</sub> protons, a singlet at δ 7.191 due to the C<sub>3</sub>-H proton and the remaining aromatic protons are appeared in the region of δ 7.109-7.867. The <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) spectrum of **5b** showed the presence of 20 carbon signals. Based on the spectral data, we have assigned the obtained product as 9-Nitro-11-phenyl-4,5-dihydro-2*H*-pyrazolo[3,4-*a*]acridine (**5a**). The identities of all of the compounds (**Table. 3**) were verified by IR and NMR spectroscopic methods, elemental analysis. The structures of pyrazolo[3,4-*a*]acridine derivatives **5a** and **5b** were unambiguously confirmed by single crystal X-ray diffraction (**Fig. 7 & 8**).

## CONCLUSION

A simple and efficient method for the synthesis of pyrazolo[3,4-*a*]acridine derivatives has been reported, which does not required high temperatures or harsh conditions. The significant features of this reaction are the mild reaction conditions, the operational



simplicity, good to high yields, and the use of an inexpensive and commercially available reagent.

## EXPERIMENTAL

Melting points (M.p.) were determined on a Mettler FP 51 apparatus (Mettler Instruments, Switzerland) and are uncorrected. They are expressed in degree centigrade ( $^{\circ}\text{C}$ ). A Nicolet Avatar Model FT-IR spectrophotometer was used to record the IR spectra ( $4000\text{--}400\text{ cm}^{-1}$ ).  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on Bruker AV 400 (400 MHz ( $^1\text{H}$ ) and 100 MHz ( $^{13}\text{C}$ )) spectrometers using tetramethylsilane (TMS) as an internal reference. The chemical shifts are expressed in parts per million (ppm). Coupling constants ( $J$ ) are reported in hertz (Hz). The terms  $J_o$  and  $J_m$  refer to ortho coupling constant and meta coupling constant. The terms s, d, t, dd refer to singlet, doublet, triplet and doublet of doublet, respectively, b s refers to a broad singlet. Microanalyses were performed on a Vario EL III model CHNS analyzer (Vario, Germany) at the Department of Chemistry, Bharathiar University. Eaton's reagent was purchased from Sigma Aldrich. Unless otherwise specified, other reagents were obtained from commercial suppliers. When known compounds had to be prepared according to literature procedures, pertinent references are given. The purity of the products was tested by TLC with plates coated with silica gel-G using petroleum ether and ethyl acetate in the ratio of 75:25 as developing solvents.

### GENERAL PROCEDURE FOR SYNTHESIS OF 9-PHENYL-3,4-DIHYDROACRIDIN-1(2*H*)-ONES (3):

A mixture of an appropriate 2-aminobenzophenone (**1**, 1 mmol) and 1,3-cyclohexanedione (**2a/2b**, 1.2 mmol) was heated for 3h in presence of freshly prepared Eaton's reagent (Phosphorus pentoxide-methanesulfonic acid) as a catalyst without any solvent at 90°C. Then the reaction mass was transferred to an excess saturated sodium carbonate solution (30 mL). The solid obtained was filtered and washed with sufficient water and extracted with EtOAc (2 × 10 mL) and dried over anhydrous magnesium sulphate. Evaporation of the solvent followed by purification on recrystallization from ethyl acetate to yield pure 9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**3**).

*7-Nitro-9-phenyl-3,4-dihydroacridin-1(2H)-one (3a)*: Yellow solid; M.p. 186-188 °C  
Yield = 89%; IR (KBr, cm<sup>-1</sup>)  $\nu_{\max}$ : 1694; 1552; <sup>1</sup>H NMR (CDCl<sub>3</sub> 400 MHz) (ppm)  $\delta$ : 2.187-2.251 (m, 2H, C<sub>3</sub>-CH<sub>2</sub>), 2.665-2.698 (m, 2H, C<sub>2</sub>-CH<sub>2</sub>), 3.334-3.366 (m, 2H, C<sub>4</sub>-CH<sub>2</sub>), 7.109- 7.129 (m, 2H, C<sub>3'</sub>, C<sub>5'</sub>-H), 7.475-7.490 (m, 3H, C<sub>2'</sub>, C<sub>4'</sub>, C<sub>6'</sub>-H), 8.112 (d, 1H, *J* = 9.20 Hz, C<sub>5</sub>-H), 8.350 (d, 1H, *J* = 2.40 Hz, C<sub>8</sub>-H), 8.435 (dd, 1H, *J<sub>m</sub>* = 2.40 Hz, *J<sub>o</sub>* = 9.20 Hz, C<sub>6</sub>-H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) (ppm)  $\delta$ : 21.02 (C<sub>3</sub>), 34.84 (C<sub>4</sub>), 40.46 (C<sub>2</sub>), 124.89 (C<sub>13</sub>), 125.02 (C<sub>10</sub>), 125.31 (C<sub>6</sub>), 126.77 (C<sub>2'</sub>, C<sub>6'</sub>), 128.05 (C<sub>3'</sub>, C<sub>4'</sub>, C<sub>5'</sub>), 128.55 (C<sub>8</sub>), 130.48 (C<sub>5</sub>), 135.80 (C<sub>1'</sub>), 145.53 (C<sub>9</sub>), 150.45 (C<sub>7</sub>), 153.21 (C<sub>12</sub>), 166.15 (C<sub>11</sub>), 197.12 (C<sub>1</sub>); Anal. Calcd. for: C<sub>19</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.66; H, 4.47; N, 8.84%.

#### GENERAL PROCEDURE FOR SYNTHESIS OF (Z)-2-(HYDROXYMETHYLENE)-9-PHENYL-3,4-DIHYDROACRIDIN-1(2*H*)-ONES

(4):

A mixture of an appropriate 9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**3**, 1 mmol) and ethylformate(1.2 mmol) was added to freshly prepared sodium methoxide (1g sodium in 10mL methanol) at 0°C to room temperature for 4-5h. Subsequently the reaction mixture was quenched with ice water (45 mL) and extracted with EtOAc (2 × 10 mL) and dried over anhydrous magnesium sulphate. Evaporation of the solvent afforded yellow solid which was recrystallized from ethyl acetate to give (Z)-2-(hydroxymethylene)-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**4**).

*(Z)*-7-Nitro-2-(hydroxymethylene)-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**4a**):

Brownish yellow solid; M.p. 124-126 °C Yield = 73%; IR (KBr, cm<sup>-1</sup>)  $\nu_{\max}$ :

3435,1693,1563; <sup>1</sup>H NMR (CDCl<sub>3</sub> 400 MHz) (ppm)  $\delta$ : 2.610-2.642 (m, 2H, C<sub>3</sub>-CH<sub>2</sub>), 3.261-3.291 (m, 2H, C<sub>4</sub>-CH<sub>2</sub>), 7.074-7.093 (m, 3H, CHOH, C<sub>3'</sub>, C<sub>5'</sub>-H), 7.338 (d, 1H, *J* = 2.00 Hz, C<sub>9</sub>-H), 7.428-7.440 (m, 3H, C<sub>2'</sub>, C<sub>4'</sub>, C<sub>6'</sub>-H), 7.597 (dd, 1H, *J<sub>m</sub>* = 2.00 Hz, *J<sub>o</sub>* = 8.80 Hz, C<sub>6</sub>-H), 7.910 (d, 1H, *J<sub>o</sub>* = 8.80 Hz, C<sub>5</sub>-H), 14.240 (s, 1H, CHOH); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) (ppm)  $\delta$ : 29.471 (C<sub>3</sub>), 34.525 (C<sub>4</sub>), 113.845 (C<sub>2</sub>), 122.654 (C<sub>13</sub>), 125.463 (C<sub>8</sub>), 127.783 (C<sub>7</sub>), 128.847 (C<sub>4'</sub>), 129.336 (C<sub>3'</sub>, C<sub>5'</sub>), 129.549 (C<sub>2'</sub>, C<sub>6'</sub>), 130.439 (C<sub>10</sub>), 131.467 (C<sub>5</sub>), 132.352 (C<sub>6</sub>), 134.023 (C<sub>9</sub>), 146.312 (C<sub>1'</sub>), 150.457 (C<sub>12</sub>), 153.210 (C<sub>11</sub>), 166.154 (CHOH), 180.120 (C<sub>1</sub>); Anal. Calcd. for: C<sub>20</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.41; H, 4.02; N, 8.13%.

**GENERAL PROCEDURE FOR SYNTHESIS OF 11-PHENYL-4,5-DIHYDRO-2H-PYRAZOLO[3,4-A]ACRIDINES (**5**):**

A mixture of an appropriate (Z)-2-(hydroxymethylene)-9-phenyl-3,4-dihydroacridin-1(2H)-one (**4**, 1 mmol) and hydrazine hydrate (1.2 mmol) was refluxed in 20 mL ethanol for 2-3 h. Then the reaction mixture was quenched with water and 1:1 HCl afforded yellow solid which was recrystallized from ethanol to furnish 11-phenyl-4,5-dihydro-2H-pyrazolo[3,4-a]acridine (**5**).

*9-Nitro-11-phenyl-4,5-dihydro-2H-pyrazolo[3,4-a]acridine (5a)*: Brownish yellow solid; M.p. 186-188 °C Yield = 63%; IR (KBr,  $\text{cm}^{-1}$ )  $\nu_{\text{max}}$ : 3385, 1625, 1554;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz) (ppm)  $\delta$ : 2.610-2.642 (m, 2H,  $\text{C}_4\text{-CH}_2$ ), 3.083-3.267 (m, 2H,  $\text{C}_5\text{-CH}_2$ ), 7.109 (d, 1H,  $J = 2.40$  Hz,  $\text{C}_{10}\text{-H}$ ), 7.191 (s, 1H,  $\text{C}_3\text{-H}$ ), 7.269-7.323 (m, 2H,  $\text{C}_2'$ ,  $\text{C}_6'\text{-H}$ ), 7.399-7.561 (m, 4H,  $\text{C}_3'$ ,  $\text{C}_4'$ ,  $\text{C}_5'$ ,  $\text{C}_8\text{-H}$ ), 7.867 (d, 1H,  $J = 8.80$  Hz,  $\text{C}_7\text{-H}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz) (ppm)  $\delta$ : 21.27 ( $\text{C}_4$ ), 34.08 ( $\text{C}_5$ ), 120.45 ( $\text{C}_7$ ), 125.84 ( $\text{C}_{10}$ ), 127.27 ( $\text{C}_{13}$ ), 127.94 ( $\text{C}_{12}$ ), 128.08 ( $\text{C}_8$ ), 128.60 ( $\text{C}_{14}$ ), 128.84 ( $\text{C}_3'$ ,  $\text{C}_4'$ ,  $\text{C}_5'$ ), 129.02 ( $\text{C}_2'$ ,  $\text{C}_6'$ ), 130.21 ( $\text{C}_7$ ), 131.35 ( $\text{C}_3$ ), 132.39 ( $\text{C}_9$ ), 137.40 ( $\text{C}_{11}$ ), 145.98 ( $\text{C}_{11}$ ), 146.77 ( $\text{C}_{16}$ ), 152.68 ( $\text{C}_{15}$ ); Anal. Calcd. for:  $\text{C}_{20}\text{H}_{14}\text{N}_4\text{O}_2$ : C, 70.17; H, 4.12; N, 16.37. Found: C, 70.12; H, 4.17; N, 16.33%.

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## SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website. Please make the words "publisher's website" a live DOI link.

Complete CIF files for compounds **3a**, **3c**, **3f**, **4c**, **4d**, **5c** and **5d** have been deposited with the Cambridge Crystallographic Data Centre as CCDC number 1009510, 984318, 1047623, 1009511, 1046857, 1019265 and 1046856 respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. [Fax: +44 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

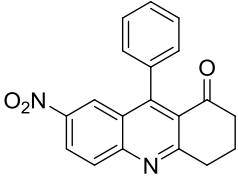
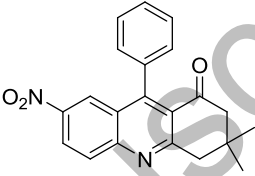
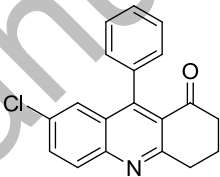
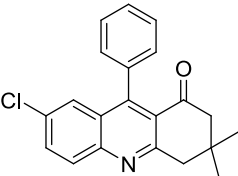
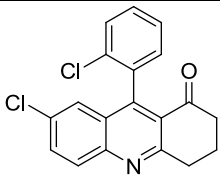
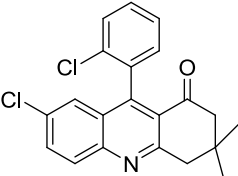
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**Table 1** Synthesis of 3,4-dihydroacridin-1(2*H*)-one derivatives (**3a-f**)

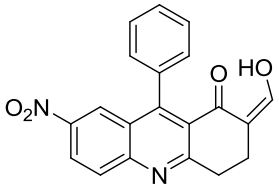
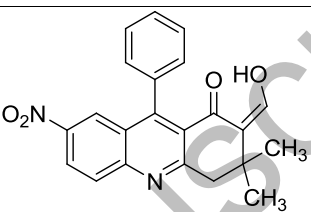
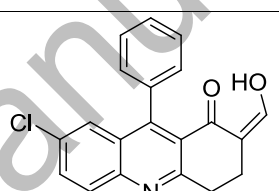
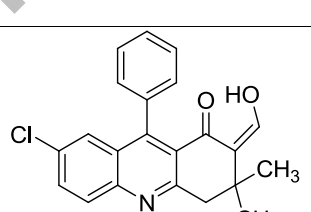
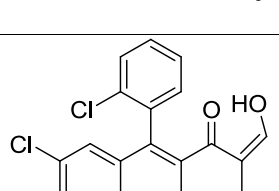
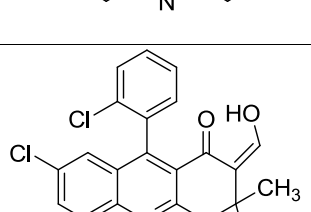
Entry	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Product	Yield <sup>a</sup>
3a.	NO <sub>2</sub>	H	H		89%
3b.	NO <sub>2</sub>	H	CH <sub>3</sub>		90%
3c.	Cl	H	H		93%
3d.	Cl	H	CH <sub>3</sub>		93%
3e.	Cl	Cl	H		85%
3f.	Cl	Cl	CH <sub>3</sub>		87%

Reaction conditions: 5-chloro-2-aminobenzophenone **1a** (1 mmol) and 1,3-cyclohexanedione **2a** (1.2 mmol, 1.2 equiv.) in the presence of Eaton's reagent as a catalyst without solvent at 90°C.

<sup>a</sup>Recrystallised pure products.



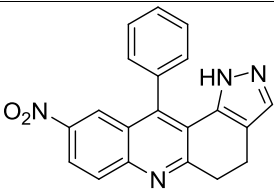
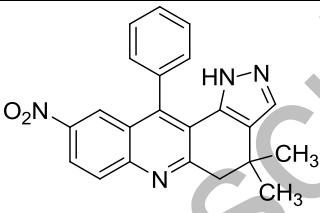
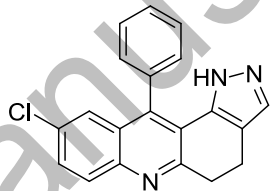
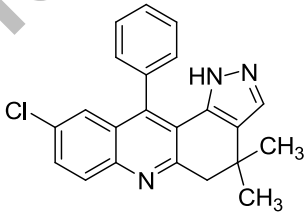
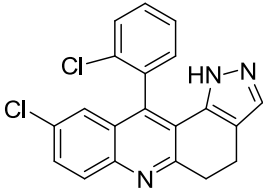
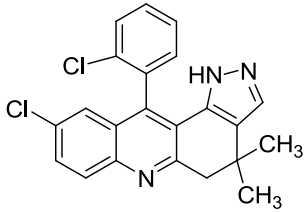
**Table 2** Synthesis of hydroxymethylene derivatives of 3,4-dihydroacridin-1(2*H*)-one (**4a-f**)

Entry	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Product	Yield <sup>a</sup>
4a.	NO <sub>2</sub>	H	H		73%
4b.	NO <sub>2</sub>	H	CH <sub>3</sub>		70%
4c.	Cl	H	H		75%
4d.	Cl	H	CH <sub>3</sub>		77%
4e.	Cl	Cl	H		75%
4f.	Cl	Cl	CH <sub>3</sub>		73%

Reaction Conditions: 7-chloro-9-phenyl-3,4-dihydroacridin-1(2*H*)-one (**3a**) (1 mmol) and ethylformate(1.2 mmol, 1.2 equiv.) in the presence of sodium methoxide at 4-5h in RT.

<sup>a</sup>Recrystallised pure products.

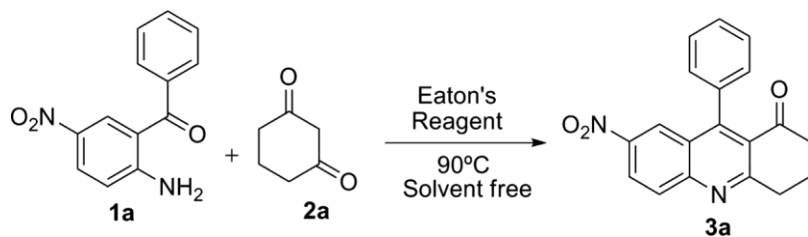
**Table 3** Synthesis of pyrazolo[3,4-*a*]acridine derivatives (**5a-f**)

Entry	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Product	Yield <sup>a</sup>
5a.	NO <sub>2</sub>	H	H		63%
5b.	NO <sub>2</sub>	H	CH <sub>3</sub>		60%
5c.	Cl	H	H		65%
5d.	Cl	H	CH <sub>3</sub>		63%
5e.	Cl	Cl	H		60%
5f.	Cl	Cl	CH <sub>3</sub>		62%

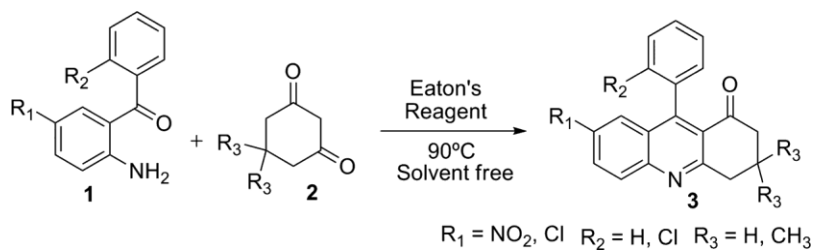
Reaction Conditions: (Z)-7-Chloro-2-(hydroxymethylene)-9-phenyl-3,4-dihydroacridin-1(2H)-one (**4a**) (1 mmol) and Hydrazine hydrate (1.2 mmol, 1.2 equiv.) in the presence of ethanol at reflux temperature.

<sup>a</sup>Recrystallised pure products.

**Scheme 1.** Synthesis of 7-Nitro-9-phenyl-3,4-dihydroacridin-1(2*H*)-ones (**3a**)

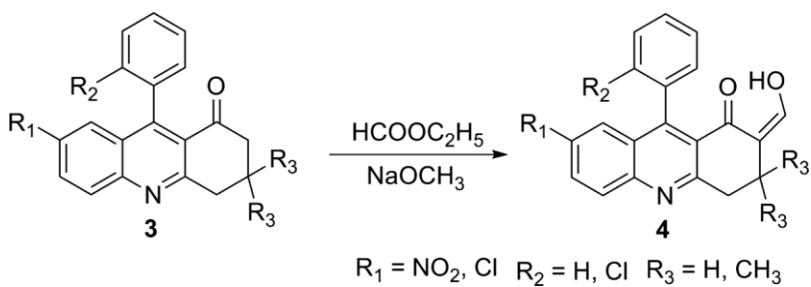


**Scheme 2.** Synthesis of 3,4-dihydroacridin-1(2*H*)-ones (**3**)

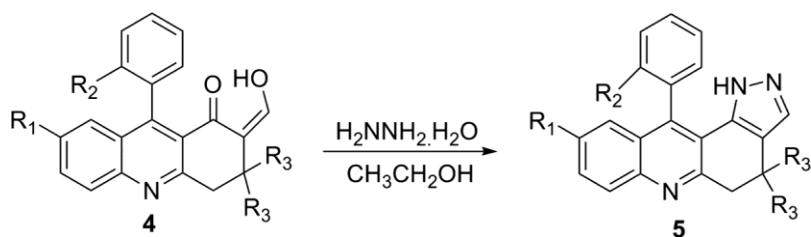


**Scheme 3.** Synthesis of Hydroxymethylene derivatives of 3,4-dihydroacridin-1(2*H*)-ones

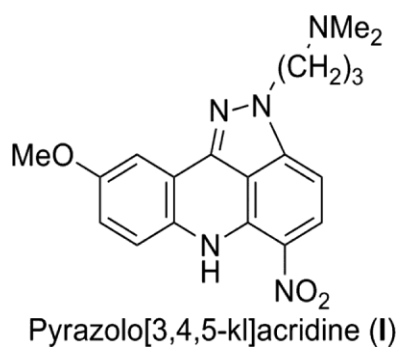
(4)



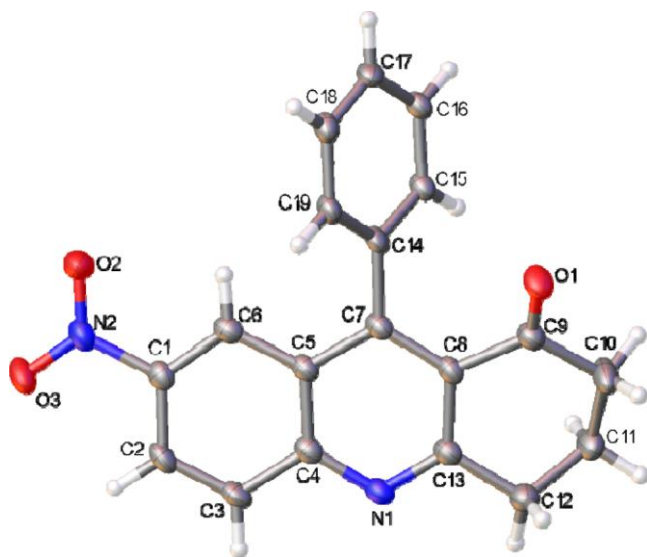
**Scheme 4.** Synthesis of Pyrazolo[3,4-*a*]acridine derivatives (**5**)



**Figure 1.** Pyrazolo[3,4,5-*kl*]acridine Scaffold for using clinical trial compounds

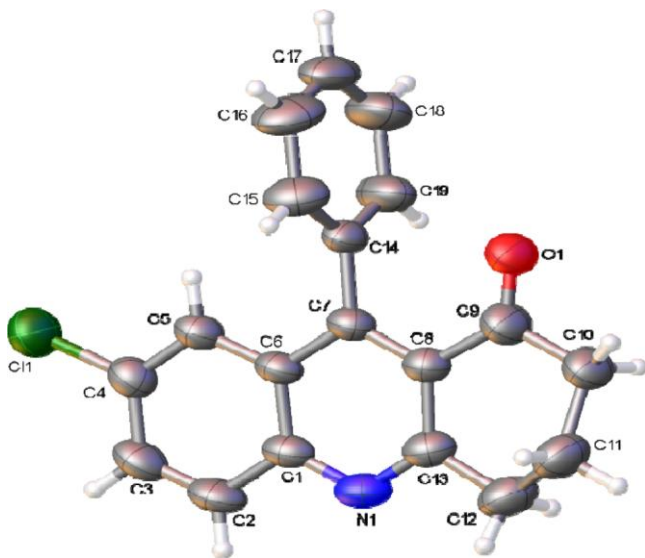


**Figure 2.** X-ray crystal structure of **3a**, Thermal ellipsoids is depicted at the 50% probability level.



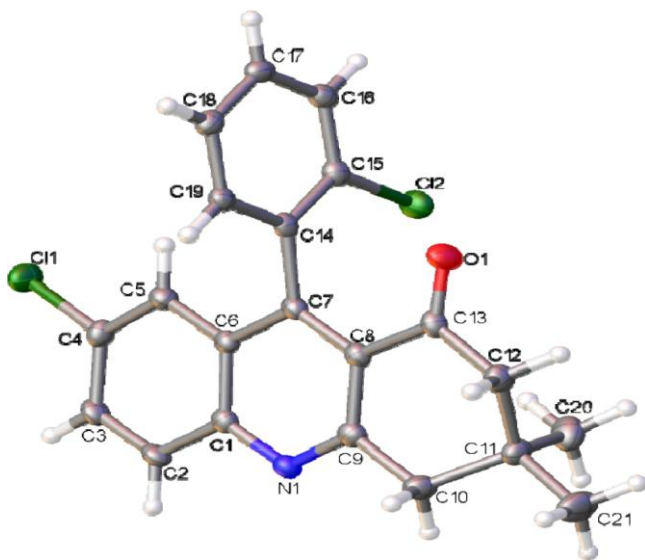


**Figure 3.** Room temperature structure of **3c** with ellipsoids depicted at the 50% probability level. The material underwent a destructive phase transition upon cooling. The structure exhibits disorder in the phenyl ring (C14-C19) and (C8-C13) ring.

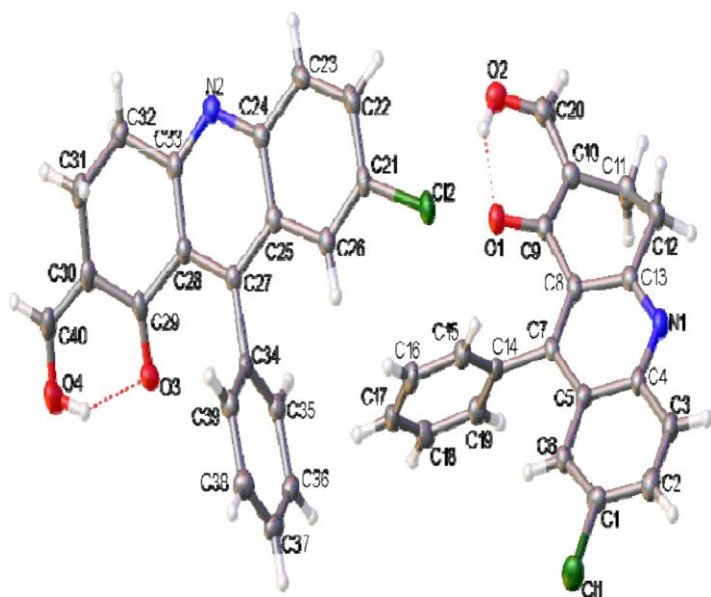


**Figure 4.** X-ray structure of **3f** with ellipsoids depicted to the 50% probability level.

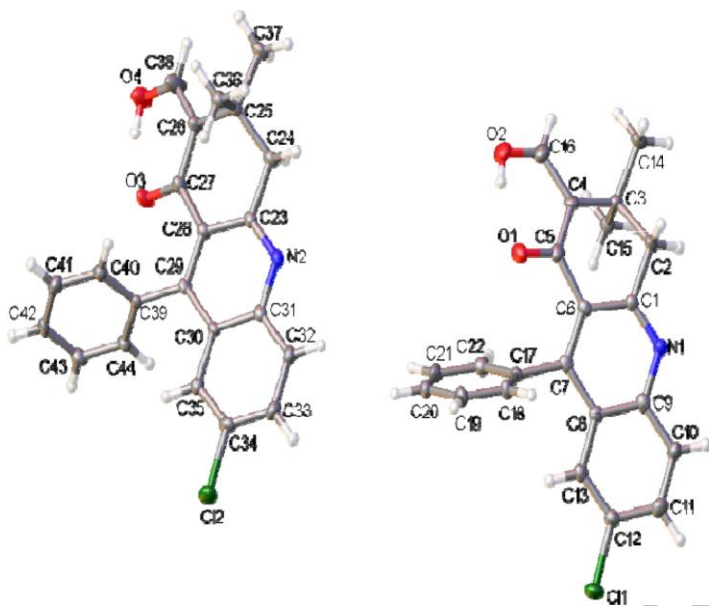
Only one position of the disordered (C14-C19) Cl2 ring has been shown for clarity.<UL>



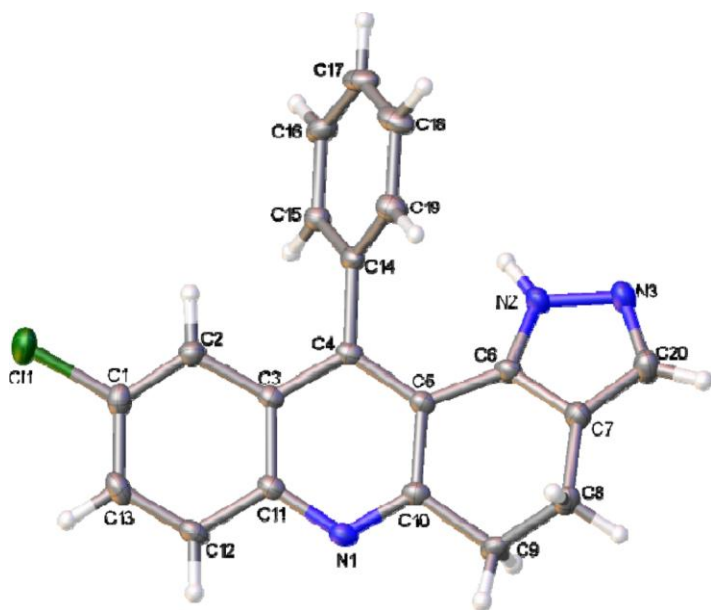
**Figure 5.** X-ray crystal structure of **4c**. Thermal ellipsoids depicted at the 50% probability level.



**Figure 6.** X-ray crystal structure of **4d**, thermal ellipsoids depicted at 50% probability level.



**Figure 7.** X-ray crystal structure of **5c**, thermal ellipsoids is depicted at the 50% probability level.



**Figure 8.** X-ray crystal structure of **5d**, thermal ellipsoids depicted at the 50% probability level.

